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ORTHODONTICELL CLINICAL PROTOCOL
USE OF BIOELECTRIC STIMULATION TO ACCELERATE TOOTH MOVEMENT IN PATIENTS WEARING BRACES

Background:
Dental malalignment is a very common problem, with several treatment options that offer variable success in achieving desired alignment. This includes primarily the use of braces and retainers that often require 18 months of wear, but offer little to no ability to retain the teeth in the new alignment.
Research has led to identification of the molecular basis of tooth movement(RANKL) and fixation(OPG). This knowledge has become the basis for the development of a new treatment option that is based on the use of programable bioelectric stimulation (BES) to significantly increase the local tissue expression of the RANKL and OPG at the desired times to enhance standard orthodontic care(braces) that shortens the time needed for wearing braces from 18 to only 6 months.

GOAL:
The goal of this study is to demonstrate equivalent safety and superior ability of BES to markedly shorten the time required for desired teeth movement.

Description:
This will be a prospective, randomized, open label, multi-arm study comparing measured tooth movement after two months of standard management for application of braces, versus use of aligner trays, with or without additional use of Bioelectric Stimulation (BES). All subjects will receive a personal BES appliance, but only the group randomized to aligners plus BES will receive actual stimulation, while the other subjects will have sham simulation of activating the stimulator. The BES will be delivered via an appliance with embedded electrodes that fits over braces or aligners and connected to an external stimulator.

The study, including the protocol and consent form will have been approved without stipulations by a local or certified Institutional

Review Board as meeting safe and good clinical practice before any subject will be enrolled.

Inclusion Criteria:

1. Age 18-30 yrs of age
2. Have moderate degree of malalignment of maxilla, mandible, or both
3. Must speak, read, and understand English
4. Able and willing to give informed consent and follow study instructions.
5. Able to tolerate up to 20 minutes of BES at the lower intensity
6. Able and willing to make the required study visits.

Exclusion Criteria:

1. Allergic to lidocaine or epinepherine
2. Individuals with diminished decision-making capacity
3. Pregnancy or lactating period for females

Study Type: Open label, Single Arm, Prospective Registry
Target Number of Participants: 30
Target Number of Enrolling Sites: 2

Length of Treatment: 2 months
Frequency of Treatments: 2 x's/week
Duration of Each Treatment: 20 minutes
Total number of Treatments: 16
Location of Treatments: All treatments will take place in the office of the Orthodontist conducting this study.

Screening Evaluation of Bioelectric Stimulator:

All subjects will have a mouthpiece placed over their braces or aligner tray which is then connected to the Mettler bioelectric stimulator., that has been previously tested and proven to be capable of delivering the required signals. The current from the stimulator will be gradually increased in intensity to define the level (1-5) that is comfortable for

that patient, and will be the intensity level used for that patient throughout the study at each treatment. If well tolerated, the patient will be eligible to participate in the Registry.

Treatment:
Each enrolled patient will return to the office of the Orthodontist conducting the study for the required treatments set forth above, which will be the same throughout the study.

Follow Up Evaluations:
Images of the teeth will be obtained at 1 and 2 months of treatment measure and document the response to treatment.
End Points:

Co-Primary Outcome Measure:
1. Increase tooth movement
2. Incidence of treatment-related adverse events by the end of the treatment period, to include, but not exclusively: local pain, signs of inflammation or irritation on the gums.

The Registry will be paused if a total of 3 of the study subjects experience a treatment-related side effect of at least moderate severity. It will be restarted when additional investigation yields a clear cause and effective action plan has been implemented.

Data Analysis:

Data will be collected for each patient and analyzed at three time points including the end of the first 50 patients, the end of 100 patients, and when the last enrolled individual has reached the 6 month post treatment time point. The Registry may be stopped if the data demonstrates a > 50 % improvement in tooth movement.